International Journal of Applied Pharmaceutical Sciences and Research

Original Research http://dx.doi.org/10.21477/ijapsr.v1i2.10944

Detection of type of thalassemia disease in patients: A fuzzy logic approach

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Article History:

Received: 16 June 2016
Accepted: 18 June 2016
Available online: 4 June 2016

Keywords: Mean Corpuscular Hemoglobin (MCH), Mean corpuscular volume (MCV); Fuzzy logic approach; Mamdani Fuzzy Inference System, Thalassemia Disease.

ABSTRACT:

In this paper, we have determined the severity of Thalassemia disease in a patient with the help of their Red Blood Cell (RBC) indices components such as Mean Corpuscular Hemoglobin (MCH) and Mean corpuscular volume (MCV). Also level of blood (Hemoglobin) is considered. We use a fuzzy application, the Mamdani Fuzzy Inference System (FIS) to generate a model for Thalassemia diagnosis. Obtained model is applied on set of data such that 15 results are similar and 3 are marginally off. It shows that the accuracy of the proposed system is 83.3%. Sensitivity analysis is carried out the result of which shows that the developed Thalassemia diagnosis model is more stable. From the viewpoint of an end-user, the results of this work can facilitate laboratory work by reducing the time and cost.

1. Introduction

The work with similar concept was already published previously, related to the Thalassemia Fuzzy model (Thakur et al., 2016). Therefore, in this study authors considered similar concept to determine more accurate results for Thalassemia disease diagnosis. Thalassemia is a genetic disease, the major form or severe form of Thalassemia is also known as Cooley's Anemia and Mediterranean Anemia (Loukopoulas et al 2011; Olivieri et al., 2011; Atkin et al., 1998; Cao et al., 2010). Introduction and complication of Thalassemia-gene and Thalassemia disease in children where provided by Cooley et al 1927; Weatherall et al., 1981; Ghodekar et al., 2010; Trent et al., 2006; Nienhuis et al., 2012; Adeyemo et al., 2011 and Madhok et al., 2014 . About 100,000 babies worldwide are born with severe forms of thalassemia each year. In India, approximately 30 million people are carrying the defective gene with carrier frequency ranging from 3% to 17% (Rakholia et al., 2013). In this study, the parameters such as Mean Corpuscular Hemoglobin (MCH), Mean corpuscular volume (MCV) and Hemoglobin (HGB) are considered to identify the type of Thalassemia in a patient. The parameters are also known as haematological parameters (Yousafzai et al., 2010).

Thalassemia is becoming a global health problem. The need to design intelligent systems that would support physicians in the medical diagnosis of the disease cannot be overemphasized. In this study, the authors presented an improvement of the previous study (Thakur et al., 2016), such that the obtained results are more stable. From the viewpoint of an end-user, the results of this work can facilitate laboratory work by reducing the time and cost.

1.1 Applications of Fuzzy Logic in disease diagnosis areas

Fuzzy logic, a powerful tool used to handle imprecision and uncertainty can be used to deal with the concept of partially true and partially false values aiming at tractability, robustness and low cost-solutions for real world challenges. Lotfi A. Zadeh in 1965 (Zadeh et al., 1965) of the University of California at Berkelely published fuzzy sets. In 1965 the fuzzy logic concepts are starting from fuzzy set theory. In 1973 Zadeh introduces the seminal work on fuzzy algorithms which introduced

the idea of formulating the control algorithm by logical rules (Zadeh et al., 1973). Then Mamdani in 1975 applied the fuzzy logic in a practical application to control an automatic steam engine, which is almost ten years after the fuzzy theory was invented (Mamdani et al., 1975). It is the biggest success of fuzzy logic in the field of industrial and commercial applications and has been achieved with fuzzy controllers. It has been developed by Ebrahim "Abe" Mamdani and his student Sedrak Assilian in 1975. In 1976 MYCIN, an early expert system, or artificial intelligence (AI) program, for treating blood infections was developed. In 1972 work began on MYCIN at Stanford University in California. MYCIN would attempt to diagnose patients based on reported symptoms and medical test results. It was the first well known medical expert system developed by Shortleaf at Stanford University IN 1976 to help doctors for blood infections (Shortliffe, 1983).

In the past couple of decades Fuzzy Inference System has proven to be an extremely efficient decision support system in a wide range of different domains (from industrial engineering to finance and health care). Most of the papers dealing with peritonitis diagnosis using computational and mathematical methods are focused on the application of statistical methods (Terg et al., 2009; Mulhern et al., 1995; Chow et al., 2005; Chow et al., 2006). Fuzzy Expert System has been constructed and used for diagnosis. Especially in the field of cardiovascular disease diagnosis, asthma, abdominal pain, tropical diseases, neurological diseases, medical analogy of consumption of drugs, malaria diagnosis, diagnosis and treatment of diabetes disorder, male impotence, syndrome differentiation, diagnosis of lung and liver diseases, prostate diseases, lymph diseases, monitoring and control in intensive care units and operation theatres, diagnosis of chronic obstructive pulmonary diseases, diagnosis of cortical malformation, etc. (Tiwari et al., 2011). There are many papers published related to the diagnosis of various diseases.

2. Materials and Methods

We describe the designing of the Fuzzy Inference System (FIS) for Thalassemia disease diagnosis.

2.1 Design of a fuzzy logic system for thalassemia disease diagnosis

Problem Specification & Define linguistic Variables: There are 3 input variables and 1 output variable.

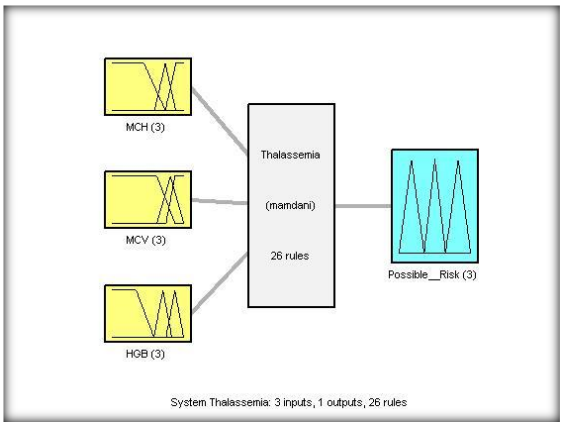


Figure 1: Mamdani fuzzy inference system for thalassemia diagnosis

2.2 Ranges for input/output fields of the system

Linguistic Variables:

- For Input Variables

Table 1: Linguistic Variable for Input Variables

S. No.	Input Variables	Linguistic Variables
1.	Mean corpuscular hemoglobin (pg)	MCH
2.	Mean Corpuscular Volume (fl)	MCV
3.	Hemoglobin (g/dl)	HGB

- For Output Variables

Table 2: Linguistic Variables for Output Variables

S. No.	Output Variable	Linguistic Variables
1.	Thalassemia Type	Possible__Risk

Define Fuzzy Sets:

- Input Variables & Value Ranges:

Table 3: Values for all Input Linguistic Variables

S. No.	Linguistic Variables	Ranges	Values
1.	MCH	<20 pg	HRI
		16-24 pg	MRI
		>20 pg	LRI
2.	MCV	< 70 fl	HRI
		50-80 fl	MRI
		>60 fl	LRI
3.	HGB	< 7 grams/deciliter	HRI
		7 – 10 grams/deciliter	MRI
		9 – 12 grams/deciliter	LRI

HRI=High Risk Intervals, MRI=Moderate Risk Intervals, LRI=Low Risk Intervals.

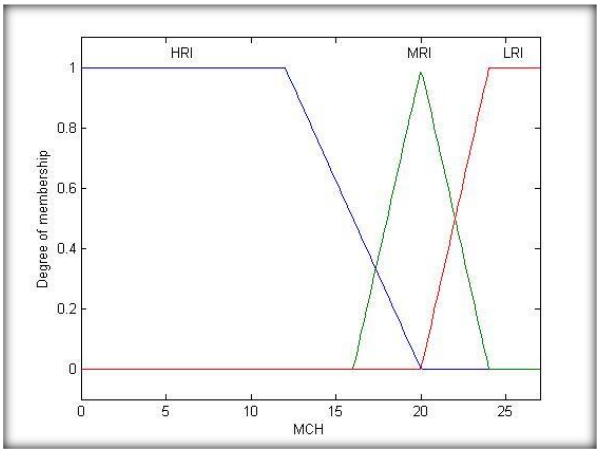
- Output Variables and Value Ranges:

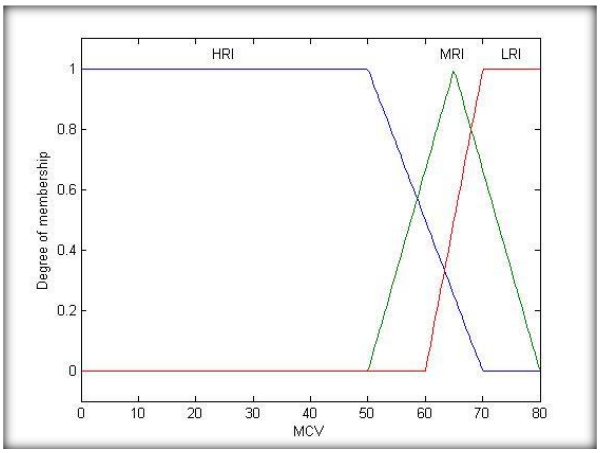
Table 5: Values for all Output Linguistic Variables

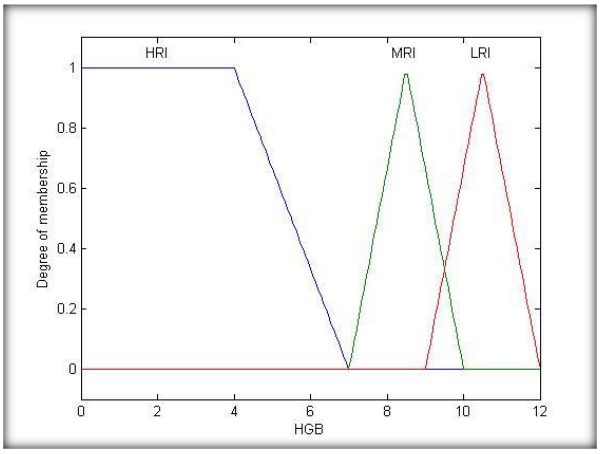
S. No.	Linguistic Variables	Ranges	Values
1.	Possible_Risk	HGB is 9 –12 g/dl	Thalassmia_Minor [Grow et al., 2014; Anunchai et al., 2011]
		MCV is <80 fl	
		MCH is <27 pg	
2.		HGB is 7 –10 g/dl	Thalassemia_Intermedia [Galanello et al., 1979]
		MCV is 50 – 80 fl	
		MCH is 16 – 24 pg	
3.		HGB is < 7 g/dl	Thalassemia_Major [Galanello et al., 1979]
		MCV is >50 <70 fl	
		MCH is >12 <20 pg	

2.3 Membership Functions

In this section membership functions of the variables are presented.







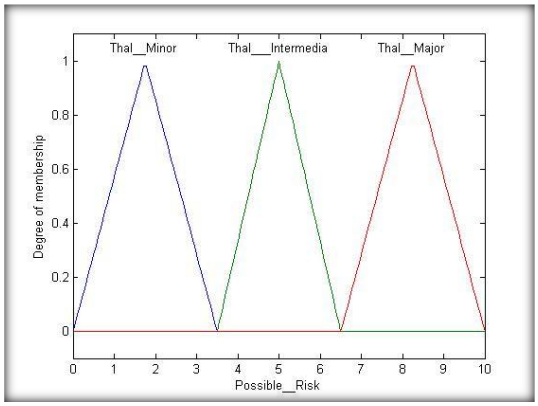


Figure 2: Fuzzy Membership for all Input and Output Variables

2.4 Output Variable

The output will be a value within the range [0, 10]. The value 0 means that no Thalassemia problems exist as of yet. We have divided this range into smaller fuzzy sets to make a cluster of type of Thalassemia disease. 'Thal_Minor' (Thalassemia Minor) is given to those patients whose output value is in between 0 and 3.5 'Thal_Intermedia' (Thalassemia Intermedia) is given to the patients who gets a value between 3.5 and 6.5 also 'Thal_Major' (Thalassemia Major) is given to the patients who gets a value between 6.5 and 10 as shown in the Table 5, The basic relationship is that the higher the severity of Thalassemia disease, the higher the output value.

Table 6: Classification of Output

S. No.	Linguistic Variable	Ranges	Fuzzy Set
1.	Possible_Risk	0-3.5	Thal_Minor
		3.5-6.5	Thal_Intermedia
		6.5-10	Thal_Major

2.5 Define Fuzzy Rules:

In this section fuzzy inference rules generated; relevant inference rules can be determined by experience human operators well, we use IF ELSE conditions for fuzzy inference rules, as we have three input variables. Also, there are 26 rules conveniently are represented in IF-ELSE Form:

2.5.1 All rules of Thalassemia diagnosis are considered as the following form: (1)

1. If (MCH is HRI) and (MCV is HRI) and (HGB is HRI) then (Possible__Risk is Thal__Major) (1)
2. If (MCH is MRI) and (MCV is HRI) and (HGB is HRI) then (Possible__Risk is Thal__Major) (1)
3. If (MCH is HRI) and (MCV is MRI) and (HGB is HRI) then (Possible__Risk is Thal__Major) (1)
4. If (MCH is MRI) and (MCV is MRI) and (HGB is HRI) then (Possible__Risk is Thal__Major) (1)

5. If (MCH is LRI) and (MCV is MRI) and (HGB is HRI) then (Possible__Risk is Thal___Intermedia) (1)
6. If (MCH is HRI) and (MCV is LRI) and (HGB is HRI) then (Possible__Risk is Thal__Major) (1)
7. If (MCH is LRI) and (MCV is LRI) and (HGB is MRI) then (Possible__Risk is Thal___Intermedia) (1)
8. If (MCH is LRI) and (MCV is LRI) and (HGB is LRI) then (Possible__Risk is Thal__Minor) (1)
9. If (MCH is MRI) and (MCV is MRI) and (HGB is MRI) then (Possible__Risk is Thal___Intermedia) (1)
10. If (MCH is LRI) and (MCV is MRI) and (HGB is MRI) then (Possible__Risk is Thal__Minor) (1)
11. If (MCH is LRI) and (MCV is LRI) and (HGB is HRI) then (Possible__Risk is Thal__Minor) (1)
12. If (MCH is LRI) and (MCV is MRI) and (HGB is HRI) then (Possible__Risk is Thal___Intermedia) (1)
13. If (MCH is LRI) and (MCV is HRI) and (HGB is LRI) then (Possible__Risk is Thal__Minor) (1)
14. If (MCH is MRI) and (MCV is MRI) and (HGB is LRI) then (Possible__Risk is Thal___Intermedia) (1)
15. If (MCH is MRI) and (MCV is LRI) and (HGB is HRI) then (Possible__Risk is Thal__Major) (1)
16. If (MCH is HRI) and (MCV is MRI) and (HGB is MRI) then (Possible__Risk is Thal___Intermedia) (1)
17. If (MCH is LRI) and (MCV is HRI) and (HGB is MRI) then (Possible__Risk is Thal___Intermedia) (1)
18. If (MCH is MRI) and (MCV is LRI) and (HGB is LRI) then (Possible__Risk is Thal__Minor) (1)
19. If (MCH is MRI) and (MCV is HRI) and (HGB is MRI) then (Possible__Risk is Thal___Intermedia) (1)
20. If (MCH is HRI) and (MCV is LRI) and (HGB is MRI) then (Possible__Risk is Thal__Minor) (1)
21. If (MCH is LRI) and (MCV is MRI) and (HGB is LRI) then (Possible__Risk is Thal__Minor) (1)
22. If (MCH is MRI) and (MCV is HRI) and (HGB is LRI) then (Possible__Risk is Thal___Intermedia) (1)
23. If (MCH is HRI) and (MCV is LRI) and (HGB is LRI) then (Possible__Risk is Thal__Minor) (1)
24. If (MCH is MRI) and (MCV is LRI) and (HGB is MRI) then (Possible__Risk is Thal___Intermedia) (1)
25. If (MCH is HRI) and (MCV is LRI) and (HGB is MRI) then (Possible__Risk is Thal___Intermedia) (1)
26. If (MCH is HRI) and (MCV is HRI) and (HGB is LRI) then (Possible__Risk is Thal___Intermedia) (1)

3. Experimental Results:

For our system we use the mamdani type FIS. For each rule a degree is calculated. For aggregation the maximum is taken from all the degrees. In the defuzzification process, the centroid method is used.

Table 8: Input Values for patient

S. No.	Input Variable	Value Ranges	Ranges Selected
1.	MCH	20 pg	19<20<27
2.	MCV	69.88 fl	60 < 69.88< 70
3.	HGB	10.92 g/dl	10 < 10.92 < 11

There are 105 plots in Figure 3, nested in a single figure window. Each rule is a row of plots, and each column is a variable. The rule numbers are displayed on the left of each row. The rules can be viewed in the status line by clicking on a rule number. The first three columns of plots (the yellow plots) show the membership functions referenced by the antecedent, or the if-part of each rule. The fourth column of plot (the blue plots) shows the membership functions referenced by the consequent, or the then-part of each rule. The plots which are blank in the if-part of any rule correspond to the characterization of none for the variable in the rule. The last plot in the fourth column of plots represents the aggregate weighted decision for the given inference system. This decision will depend on the input values for the system. The defuzzified output is displayed as a bold vertical line on this plot. The variables and their current values are displayed on top of the columns. In the lower left, there is a text field Input for entering specific input values.

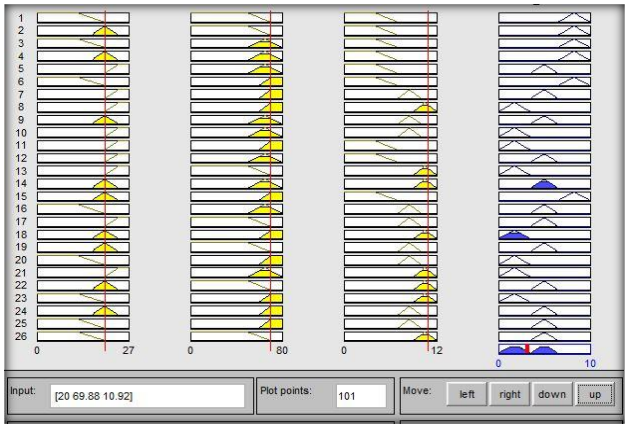


Figure 3: Rule Viewer for Generated Rules

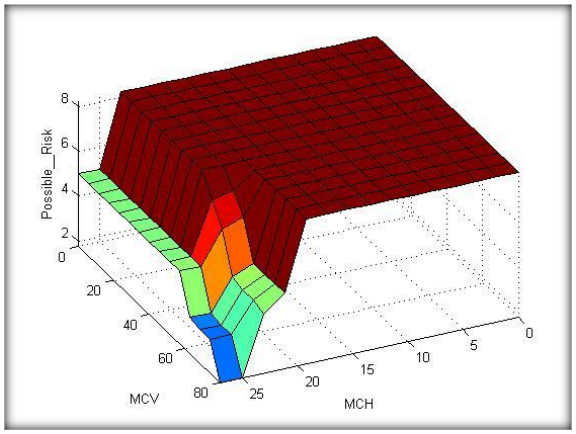


Figure 4(a)

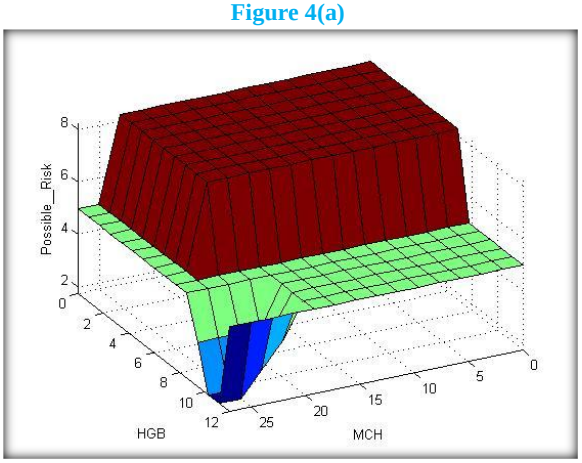


Figure 4(b)

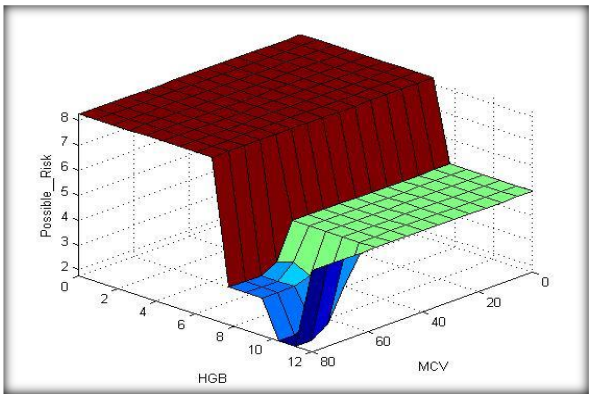


Figure 4(c)

Figure 4: A Surface Viewer plot of severity of Thalassemia disease between different inputs attributes. (a) Plot between MCV, MCH and Possible_Risk. (b) Plot between HGB, MCH and Possible_Risk. (c) Plot between HGB, MCV and Possible_Risk.

4. Result and Discussion

In Figure 4a, Figure 4b and Figure 4c the dependency of the output Possible_Risk depends on three inputs such as Mean Corpuscular Hemoglobin (MCH), Mean corpuscular volume (MCV) and Hemoglobin (HGB). In Fig. 4a, the value of MCH is belongs to HRI and the value of MCV is belongs to HRI, the output become Thal_Major, which is the most severe form of Thalassemia. In this condition patient needs lifelong regular blood transfusions and iron chelation therapy. Similarly, we can describe the other plots of system plot between HGB-MCH and HGB-MCV. Hence, all the results depend on the level of inputs such that the

severities of Thalassemia increases as the value of inputs are decreases. For cases where the level of HGB (Hemoglobin) is grater than 7, there is possibility of Thalassemia Intermedia (Thal_Intermedia) and Thalassemia Minor (Thal_Minor), which are less severe conditions than Thalassemia Major the possibility of having Thal_Major condition is depend on the value of HGB that is <7, that means the value belongs to the HRI (High Risk Interval).

We tested our fuzzy expert system against the following input variable values. To test the accuracy of our system we have taken 18 random patients' such that 15 results are similar rest of 3 results are not under the consideration. An accuracy of system is 83.3% which is more stable than the results obtained from the similar contents in (Thakur et al., 2016) with accuracy 80%.

5. Conclusion

In this work, a fuzzy based Inference System was developed in order to analyze the severity of Thalassemia disease using Fuzzy Logic Toolbox in Matlab by developing 26 if-then rules. The fuzzy system result shows that the selected inputs such as MCH, MCV and HGB are suitable for the study. Also, sensitivity analysis is carried out the result of which shows that the developed Thalassemia diagnosis model is more stable. From the viewpoint of an end-user, the results of this work can facilitate laboratory work by reducing the time and cost.

Acknowledgment

I wish to express my deep sense of gratitude to Mr. Pramod Puri, General Secretary of Thalassemia Welfare Society, Bhilai (Chhattisgarh, India), for his excellent guidance, valuable suggestion that greatly helped me to complete the work successfully.

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How to cite this article:

S. Thakur, S. N. Raw, R. Sharma, P. Mishra (2016). Detection of type of thalassemia disease in patients: A fuzzy logic approach. *Int J Appl Pharm Sci Res*. 1(2):88-95. doi: 10.21477/ijapsr.v1i2.10944